

REMARKS

Claims 15, 18-29, 63, 65, and 66 are pending in the Application. Claim 29 is amended to address typographical errors and does not contain new matter.

In the Office Communication mailed on May 26, 2010, the Examiner maintains certain rejections and raises several new rejections. For clarity, the rejections are listed below in the order in which they are addressed herein.

- I. Claims 15, 18-29, 63 and 65-66 stand rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention;
 - II. Claims 15, 18-19, 21 and 29 stand rejected under 35 U.S.C. 102 (b) as allegedly being anticipated by Egner et al (Chem. Commun., 1997);
 - III. Claims 15 and 18-21 stand rejected under 35 U.S.C. 102(e) as allegedly anticipated by or, in the alternative, under 35 U.S.C. 103(a) as allegedly obvious over Seul et al (USP 7083914);
 - IV. Claims 15, 18-29, 63 and 65-66 stand rejected under 35 U.S.C. 102(c) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as allegedly being obvious over Kauvar et al (USP 6642062) (as evidenced by Tao Jia-ping et al (Chinese Journal of Physical Medicine (Vol. 17(3), September 1995, p 168-171);
 - V. Claims 15, 18-29, 63 and 65-66 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over anyone of Egner et al or Kauvar or Seul in view of Yamashita(WO95/32425) and either Kris et al (USP 6238869) or Kimura et al (USP 6228480).
- I. Claims 15, 18-29, 63 and 65-66 stand rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding Claim 15, the Examiner asserts that it not clear as to what is included or precluded by said features or in what respect the features varies so as to be detected by any means or from one another. Applicants respectfully disagree.

The claims are directed toward carriers, *e.g.*, beads, for use as supports in combinatorial synthesis of compounds, *e.g.*, of polymers such as polypeptides or oligonucleotides, that have

detectable, distinctive features (also referred to in the specification as attributes) that can be used to uniquely identify individual carriers prior to any synthesis of the compound and that can be used to track particular carriers during and after synthesis (*e.g.*, split-process-recombine synthesis of a library of polymers, such as polypeptide or oligonucleotide chains). See, *e.g.*, the specification at page 6, lines 14-19. As such, the features of the carriers of the instant claims remain consistent both before and during the sequential synthesis process steps, as well as after synthesis is completed. The ability to track carriers in this manner permits the entire synthesis history of any particular product to be tracked (Specification at page 15, lines 21-23). Tracking synthesis is desirable in complex combinatorial synthesis schemes, such as the split-process-recombine procedure diagrammed in Figure 2 (the utility of such trackable carriers is not limited to this particular synthesis process.) Further, as the features must be present prior to any synthesis steps, they cannot be added during the synthesis process steps.

As discussed in the specification, one of the difficulties in tracking combinatorial synthesis products is that the number of possible products can be enormous (*e.g.*, 20^9 possible nonamer peptides; see, *e.g.*, page 1, lines 18-20), and providing a corresponding number of uniquely identifiable carriers is problematic, especially if only as single feature, such as color, is used. The instant application provides carriers that each have a plurality of detectable, distinctive features that detectably vary among a different individual carriers within the population of carriers. When pluralities of different features are analyzed, each carrier can be uniquely identified within an extremely complex mixture of carriers, by looking for the one particular combination of features associated with the carrier of interest. The combination of features is the code associated with that carrier (see Specification page 19, lines 1-4).

While a carrier may have other attributes that are not detected during identification of a carrier (*e.g.*, shape, surface deformations), the distinctive attributes that are detected or measured during identification as the code are the "features" that define the code. (see Specification page 19, lines 1-4).

Regarding Claim 15, the Examiner further asserts that it is vague and indefinite as to what aspects or manner a code corresponds to "all the features" of a carrier. Applicants respectfully disagree and, as explained above, submit that one of skill in the art would understand that the "code" simply refers to the complete set of detectable, distinctive features of a carrier selected for analysis in combination to uniquely identify one particular carrier from other carriers. As stated in Claim 15,

carriers comprise all of the features that define the code prior to the initiation of synthesis of the compound. In other words, features are not added during the steps of synthesis of the compound.

Regarding Claims 19, 23, 26, 63, 65 and 66, the Examiner asserts the claims are vague and indefinite in the recitation of "one or more" and suggests that "At least" would be a better phrasing. For business reasons and without acquiescing to the Examiner's arguments, and reserving the right to prosecute the original or similar claims in one or more future applications, Claims 19, 26, 63, 65 and 66 are herein amended to recite "at least." Claim 23 does not recite "one or more" and does not require amendment.

Regarding Claim 19, the Examiner asserts that the claim is vague and indefinite as to the illumination of the carrier with "selected vectors". For business reasons and without acquiescing to the Examiner's arguments, and reserving the right to prosecute the original or similar claims in one or more future applications, Claim 19 is amended herein to delete reference to "selected vectors."

Regarding Claim 65, the Examiner asserts that this claim is inconsistent with Claim 15, from which it depends. The Examiner notes that the base claim recites the negative limitation of the features of the carrier not being based on shape, and Claim 65 recites said features as shape. Applicants respectfully disagree that this is inconsistent. Claim 15 indicates that the carrier must have at least two non-shape related features. However, the negative limitation does not preclude additional features, *e.g.*, features 3, 4, 5,etc. from being based on shape.

The Examiner asserts that Claim 15 is vague and indefinite and that it is allegedly unclear whether the code that distinctively identifies a carrier before, during and after a combinatorial synthesis from other carriers is different in each stage of the combinatorial synthesis. Applicants respectfully submit that Claim 15 is clear. Nonetheless, for business reasons and without acquiescing to the Examiner's arguments, and reserving the right to prosecute the original or similar claims in one or more future applications, Claim 15 is herein amended to recite "wherein said code is the same before, during and after said combinatorial synthesis".

The claims are not anticipated

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. MPEP 2131, citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d. 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

II. Claims 15, 18-19, 21 and 29 stand rejected under 35 U.S.C. 102 (b) as allegedly being anticipated by Egner et al (Chem. Commun., 1997. Egner discloses the use of single dyes to color beads, and discloses the use of a fluorescence microscope to resolve ambiguities between the colored beads (page 735, column 1). Egner also discusses the use of a number of fluorescent dyes together with spectrum deconvolution to provide a sensitive dye coding system for the beads. The Examiner asserts that Egner thus discloses a plurality of carriers with at least two detectable features (Office Action page 5). Applicants respectfully point out that different fluorescent dye labels providing different colors are not different “features.” Rather, they are variations of the same feature (molecular fluorescence). As such, the use of different dyes or combinations of dyes to produce different emission spectra does not provide the “at least two” features of the claims (unamended) or the “at least three” features if the claims as presently amended. As previously noted (Response of April 13, 2010), Enger does not teach that the Raman scattering observed was or could be used in combination with molecular fluorescence as a second “feature” defining a distinctive code. In fact, Egner does not teach or even suggest that Raman scattering provides any useful means of distinguishing one bead from another. As such, the Raman scattering disclosed by Egner does not have the properties required by the “light scattering feature” of the claims.

Applicants maintain the arguments made in the Amendment and Response filed on April 13, 2010. Egner does not teach the elements of the instant claims.

For business reasons and without acquiescing to the Examiner's arguments, and reserving the right to prosecute the original or similar claims in one or more future applications, Claim 15 is amended herein to recite that each carrier in the plurality of distinctively identifiable carriers comprises at least three light emanating features, and that these light emanating features comprise 1) two light scattering features and 2) a molecular fluorescence feature, wherein said light scattering features comprise light side scattering and light forward scattering as determinable by flow cytometry. Support for this amendment is found, e.g., at page 28, lines 4-7. While not acquiescing that Egner teaches or suggests the other elements of Claim 15 and the claims depending therefrom, Egner does not teach or suggest carriers having at least two light scattering features comprising light side scattering and light forward scattering as determinable by flow cytometry. As such, Egner does not anticipate Claims 15, 18-19, 21 and 29 and

Applicants respectfully request that these rejections be withdrawn.

III. Claims 15 and 18-21 stand rejected under 35 U.S.C. 102(e) as allegedly anticipated by or, in the alternative, under 35 U.S.C. 103(a) as allegedly obvious over Seul et al (USP 7083914). In particular, the Examiner points to column 5, line 26 through column 6 line 56 and asserts that the color codes of Seul encompass the light emitting features of the instant claims. Applicants respectfully disagree. Applicants maintain the arguments made in the Amendment and Response filed on April 13, 2010. In particular, Applicants pointed out that the instant claims recite that each carrier has a code which distinctively identifies a respective carrier **before, during and after a combinatorial synthesis** from other carriers." As noted above, Claim 15 is further amended herein to recite that said code *is the same* before, during and after said combinatorial synthesis.

In contrast to the carriers of the instant claims, the particles of Seul are tagged during combinatorial synthesis. See, e.g., Seul at column 6, lines 47-54.

Response to Arguments:

Citing *In re Thorpe*, the Examiner argues that "the patentability of a product does not depend on its method of production or use. If the product in the product-by-process (or use) claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made (or can be used) by a different process." Office Action page 9.

As noted above, Seul adds labels during synthesis. As such, Seul never provides and does not teach or suggest a carrier that is coded prior to any compound synthesis and that maintains the same code before, during and after synthesis. As Seul does not teach or suggest the same product as that of the instant claims, Applicants respectfully submit that the holding of *In re Thorpe* is not applicable. For these reasons, Applicants respectfully submit that the claims are not anticipated by Seul and respectfully request that these rejections be withdrawn.

In the alternative, the Examiner asserts that Claims 15 and 18-21 are unpatentable under 35 U.S.C. 103(a) as allegedly being obvious over Seul. Applicants respectfully disagree. It is well-settled law that obviousness requires at least a suggestion of all of the features in a claim. See *In re Wada and Murphy*, citing *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) and *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)). As discussed above, Seul

does not teach of suggest a carrier that is coded prior to any compound synthesis and that maintains the same code before, during and after synthesis. The Examiner urges that it would have been obvious to place the labels of Seul prior to synthesis (Office Action page 10). Applicants disagree and note that Seul is wholly directed to the advantages of adding detectable dyes during the process of combinatorial syntheses. See, e.g., Claim 1, and column 6, lines 52-54. Further, Seul teaches that there are two ways in which to add fluorophores to beads and both occur during synthesis. See column 6, lines 57 to 63. Nothing in Seul would suggest to one of skill that a complete set of all fluorophores might be or should be added prior to the first step of combinatorial synthesis.

For the reasons recited above, Applicants submit Seul does not teach or suggest each of the elements of the instant claims and therefore fails to establish the obviousness of the instant claims. Applicants therefore request that these rejections be withdrawn.

IV. Claims 15, 18-29, 63 and 65-66 stand rejected under 35 U.S.C. 102(e) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as allegedly being obvious over Kauvar et al (USP 6642062) (as evidenced by Tao Jia-ping et al(Chinese Journal of Physical Medicine (Vol. 17(3), September 1995, p 168-171).

Kauvar does not teach the use of the multihued beads as a carrier for combinatorial synthesis. Rather, for combinatorial library screening, Kauvar teaches that the addition of color generating moieties..."can be carried out in conjunction with the synthesis of the library members"... (Col 9, line 35). That is, Kauvar teaches encoding the particles during the combinatorial synthesis. Applicants note that, even though Kauvar suggests coding during combinatorial synthesis, there is no disclosure of how to accomplish such coding.

As discussed above, the instant claims recite "A plurality of carriers . . . comprising a population of detectably distinct carriers . . . each carrier having a code which distinctively identifies a respective carrier **before, during and after a combinatorial synthesis** from other carriers.

Kauvar does not teach or suggest a plurality of carriers comprising a population of detectably distinct carriers . . . each carrier having a code which distinctively identifies a respective carrier **before, during and after a combinatorial synthesis** from other carriers. The Examiner cites the disclosure of Jai-ping in reference to detection of the Kauvar beads by flow

cytometry. Applicants note that the cited passage in Kauvar refers only to colors of commercially available beads resolvable by color, and respectfully point out that the fact that flow cytometry *could* be used as a basis for bead differentiation does not mean that all beads analyzed by flow cytometry can be differentiated based on, e.g., codes such as those recited in the instant claims. Neither Kauvar nor Jai-ping teach or suggest that the beads of Kauvar are - or could be - distinctively identified by a code that is the same before, during and after combinatorial synthesis, as required by the instant claims.

Citing *In re Thorpe*, the Examiner argues that "the patentability of a product does not depend on its method of production or use. If the product in the product-by-process (or use) claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made (or can be used) by a different process." Office Action page 15.

As noted above, Kauvar adds labels during synthesis. As such, Kauvar never provides and does not teach or suggest a carrier that is coded prior to any compound synthesis and that maintains the same code before, during and after synthesis. As Kauvar does not teach or suggest the same product, Applicants respectfully submit that the holding of *In re Thorpe* is not applicable to the instant claims. For these reasons, Applicants respectfully submit that the claims are not anticipated by Kauvar and respectfully request that these rejections be withdrawn.

Applicants submit that Kauvar, even if considered in view of Jai-ping, does not teach or suggest the elements of Claims 15, 18-29, 63 and 65-66, and therefore does not anticipate these claims. Applicants therefore respectfully request that these rejections be withdrawn.

VI. Claims 15, 18-29, 63 and 65-66 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over anyone of Egner et al or Kauvar or Seul in view of Yamashita(WO95/32425) and either Kris et al (USP 6238869) or Kimura et al (USP 6228480).

Applicants respectfully disagree. The teachings of Egner, Kauvar, and Seul are discussed above. For the reasons recited above, Applicants submit that none of these references teach or suggest each of the elements of the instant claims. Yamashita discloses the preparation of combinatorial libraries, which are synthesized on beads that are separated into pools or groups, wherein the beads within each group are similarly tagged and wherein each group is uniquely tagged (see page 5, lines 12 to 18). As noted in the Response filed on April 13, 2010,

Yamashita does not teach or disclose a carrier having light scattering "features" that define the code that *distinctively identifies its respective carrier*. Kris discloses the properties of certain solids. Kimura discloses the properties of certain adhesive layers and solids. Yamashita, Kris and Kimura fail to cure the deficiencies of Egner, Seul and, Kauvar.

The Examiner asserts that there is nothing new and unobvious in the claim of a plurality of carriers for combinatorial library synthesis wherein the multitude of carriers is coded to identify or differentiate one from the other. The Examiner further asserts that coding a multitude of carriers in a library which contains millions of compounds obviously facilitates identification of the synthesized compounds in the carrier. Applicants respectfully point out that the Examiner, as evidenced by the arguments relating to Seul and Kauvar, does not distinguish between coding that occurs prior to complex combinatorial synthesis coding that occurs during synthesis. As such, it appears that the Examiner fails to consider the significant technical hurdles to assembling such a high-complexity library of carriers that are coded prior to combinatorial synthesis. As noted in the specification, combinatorial synthesis produces vastly complex libraries. For example, a library of nonapeptides constructed using 20 different amino acids (*i.e.*, the synthons) could include 10^9 different library members (page 1, lines 18-20). Seul teaches the advantages of adding tags during the combinatorial synthesis because of the complexity of the resulting libraries. None of the cited references have suggested providing a plurality of carriers having the recited features for which a code can be determined prior to synthesis, and that comprise a collection of codes of sufficient diversity that individual reaction histories can be traced for each member of a combinatorial library. While it is easy to assert that the claims merely combine known elements, it remains a fact that the cited art did not make such a combination and the Examiner provides no articulated reasoning as to why one of skill in the art *at the time of filing* would have found it obvious to pre-label carriers with a detectable codes prior to combinatorial synthesis, or why one would have expected success in doing so based on the cited art.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that all grounds for rejection have been addressed and Applicants' claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (608) 662-1277.

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